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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,090	03/10/2005	Kensuke Yuuki	050148	1836

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,090	YUUKI ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-9,11-21 and 23-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5* is/are allowed.

6)☒ Claim(s) *1-3,6-9,11-17,18-21 and 23-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/12/2006 has been entered.

The amendment filed on 11/2/2006, amending claims 1, 7, 11, 13, 19, 23, 25-26, 28-29, 31-32, 34-35, and canceling claims 4, 10 and 22 is acknowledged.

Claims 1-3, 5-9, 11-21 and 23-36 are currently pending and under consideration for examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

Acknowledgement is made of applicants claim for foreign priority to application JAPAN-2002-263834 filed on 9/10/2002.

Drawings

Drawings submitted on 3/10/2005 are objected by the Examiner for the recitation of the nucleic acid and protein sequences without appropriate sequence identifiers i.e. SEQ ID NOs. Examiner urges the applicants to provide sequence identifiers in response to this Office action. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 U.S.C. § 112(2)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-3, 6-9, 11-16, 19-21, and 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 7, 11, 13, 16, 19, 23, 25-26, 28-29, 31-32, and 34-35 recite "structural gene" in the context of transglutaminase protein. The metes and bounds of the term "structural gene" are not clear to the Examiner. It is unclear to the Examiner, how transglutaminase protein can be a structural gene. There is no definition in the specification of the phrase "structural gene" as to how transglutaminase protein is a structural protein. The Examiner requests clarification.

Claims 1-3, 6-9, 11-16, 19-21, and 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 7, 11, 13, 16, 19, 23, 25-26, 28-29, 31-32, and 34-35 recite "acting on the structural gene" in the context of terminator sequence. It is unclear to the Examiner, how a terminator sequence acts on the structural gene, which is supposed to be expressed. A sequence in DNA that signals termination of transcription to RNA polymerase is the termination sequence, which does not work on structural gene but work with RNA polymerase. The Examiner requests clarification.

Claims 1-3, 6-9, 11-16, 19-21, and 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 7, 11, 13, 16, 19, 23, 25-26, 28-29, 31-32, and 34-35 recite, "which are externally introduced" in the context of a transformant

comprising a structural gene of transglutaminase, a promoter and a terminator sequence. It is unclear to the Examiner, how a transformant is made by separately introducing structural gene, promoter or terminator sequence. The structural gene, promoter and terminator sequence should be in a vector in a specific orientation and said vector comprising said gene, promoter and terminator sequence can be introduced into a microorganism to make a transformant. The Examiner requests clarification.

Withdrawn - Claim Rejections - 35 U.S.C. § 112 (1)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejection of claims 1-3, 6-9, 12-15, 18-21, 24-25 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement and on enablement issues is withdrawn in view of applicants amendments of claims and persuasive arguments.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 13-14, 16, 18-19, 20; 23-24 and 31-36 under 35 U.S.C. 102(e) as being anticipated by Taguchi et al. (WO 01/29187 A1, "Process for producing microorganism-origin transglutaminase", Ajinomoto Co., Inc., see IDS) is maintained. As

discussed previously, Taguchi et al. disclose a process for producing microorganism-origin (Streptomyces mobaraensis) transglutaminase in transformant of S. lividans and the sequence of a transglutaminase (SEQ ID NO: 3) which is 100% identical to SEQ ID NIO: 1 and the coding sequence of SEQ ID NO: 2 of the instant application. Taguchi et al. also disclose that gene is derived from S. mobaraensis with natural promoter i.e. promoter from S. mobaraensis. DNA of Taguchi et al. would hybridize with SEQ ID NO: 2 at the recited hybridizing conditions because the DNA of Taguchi et al. is 100% identical to the entire coding region of SEQ ID NO: 2 of the instant application. Taguchi et al. further disclose the cloning of the cDNA in expression vector, which includes a transcriptional terminator derived from Streptomyces azureus (tsr gene comprises terminator) and producing transformant S. lividans comprising the expression vector containing the sequence of a transglutaminase gene to produce transglutaminase in high efficiency. Taguchi et al. also mutated the transglutaminase gene and transformed S. lividans.

Applicants argue that the claims require: "a promoter and a terminator acting on the structural gent" of transglutaminase. The shuttle vector pUJ-MTG disclosed by Taguchi et al. contains the tsr gene, and the tsr gene comprises a streptomyces-specific termination signal sequence. However, this termination signal sequence acts on the tsr gene itself. In other words, this termination signal sequence is not used for a transcription of the transglutaminase gene (MTG) in the shuttle vector, which may be seen from the configuration of the shuttle vector in Fig. 1 of Taguchi et al. In contrast, the terminator recited in claims 13-14, 16, 18-19, 20, 22 and 24 acts on the structural gene of transglutaminase. This is not taught or suggested in Taguchi et al.

This is not found persuasive because Taguchi et al. indeed teach an expression vector pUJ-MTG comprising microbial transglutaminase gene as mentioned above with natural promoter and using termination signal sequence which is after the transglutaminase coding sequence (clock wise direction). A sequence in DNA that signals termination of transcription to RNA polymerase is the termination sequence, which does not work on a gene or structural gene but work with RNA polymerase. Therefore, RNA polymerase will use the signal of termination sequence for terminating mRNA synthesis of transglutaminase coding DNA if the sequence is present after the coding sequence irrespective of the presence of another gene such as tsr. The mRNA of transglutaminase will synthesize transglutaminase protein through translation process. This termination sequence is from Streptomyces species.

Thus, for the reasons above, and discussed in the previous Office actions, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Previous rejection of Claims 1-2, 6-8, 11, 12 and 25-30 under 35 U.S.C. 103(a) as being unpatentable over Taguchi et al. (WO 01/29187 A1, "Process for producing microorganism-origin transglutaminase", Ajinomoto Co., Inc., see IDS) is maintained. The rejection was explained in the previous office action. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection on obviousness issue.

Applicants argue that the motivation for combining the references is improper and stated that this motivation is based on the assumption that using the same bacterium as the source of the gene and the host would give an increased level of expression. Applicant also argues that they maintain the previously argued position that there is no basis for this assumption in the disclosure of Taguchi et al., and that the Examiner had given no basis in the general art for this assumption. Applicant also argued that Taguchi et al. does not provide the "terminator acting on the structural gene" of transglutaminase.

As discussed in the previous office action and above, Taguchi et al. disclose a process for producing microorganism-origin (S. mobaraensis) transglutaminase in a transformant and the sequence of a transglutaminase (SEQ ID NO: 3) which is 100% identical to SEQ ID NIO: 1 and

the coding sequence of SEQ ID NO: 2 of the instant application and any DNA would hybridize with SEQ ID NO: 1 at the recited high stringency hybridizing conditions. Taguchi et al. also disclose that gene is derived from S. mobaraensis with natural promoter. Taguchi et al. further disclose the cloning the cDNA in expression vector and producing transformant S. lividans (current invention is making transformant of S. lividans and S. mobaraensis) comprising the expression vector containing the sequence of a transglutaminase gene to produce transglutaminase in high efficiency. Taguchi et al. already disclose a part of the instant claimed invention but do not disclose transforming S. mobaraensis comprising sequence of a transglutaminase gene.

Contrary to applicant's arguments, Taguchi et al. indeed teach using transcriptional termination signal sequence i.e. terminator sequence from Streptomyces species. Taguchi et al teach the use of shuttle vector pUJ-MTG, which is used to make transformant, comprises microbial transglutaminase (MTG) gene, that is prepared by combining several vectors including pIJ702 vector, which is a streptomyces specific vector contains tsr gene, The tsr gene comprises a streptomyces specific termination signal sequence derived from Streptomyces azureus (see Pulido et al. Optimization of gene expression in Streptomyces lividans by a transcription terminator, NAR 15(10) 1987, p4227-4240). Furthermore, contrary to applicant's arguments a skilled artisan would have been motivated to express the transglutaminase gene of Taguchi et al. in S. mobaraensis because native regulatory factors, which are present in S. mobaraensis would activate the transcription by acting on natural promoter to produce said transglutaminase protein in increased amounts than in other host cell. Trono et al. (1990) teach that murine cells restrict human immunodeficiency virus (HIV), infection and replication, which is highly infective and

replicated in human cells. Trono et al. also teach that murine cells lack factors necessary for the assembly and release of virions as well as defects in Rev function, which binds HIV LTR promoter and activates HIV replication by enhanced production of structural and regulatory proteins, which clearly provide the evidence that HIV which is human virus unable to infect or replicate in mouse cell because mouse cell lacks factors which are present in human cell. Therefore, it would have been obvious to transform S. mobaraensis with Streptomyces specific terminator sequence as taught by Taguchi et al. Thus, for the reasons above, the rejection is maintained.

Conclusion

Status of the claims:

Claims 1-3, 5-9, 11-21 and 23-36 are pending.

Claims 1-3, 6-9, 11-16-17, 18-20 and 23-36 are rejected.

Claim 21 is objected to as dependent on rejected claim.

Claims 5 is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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